REMARKS

Reconsideration is respectfully requested in view of the foregoing amendments and the remarks which follow.

By this amendment Applicants have cancelled claims 4-9, inclusive, and claims 14, 15 and 20. Cancellation of these claims is without prejudice or disclaimer.

Claims 1-3, 10-13, and 16-19 have been amended. The amendments to these claims are fully supported in the as-filed specification.

Claims 21-24 have been added herein. These claims are also fully supported in the as-filed specification.

Thus, the claims presently pending before the Examiner are 1-3, 10-13, 16-19 and 21-24.

Claims 1 and 19 have been amended to recite the language as suggested by the Examiner and, moreover, introducing a limitation in the scope of the inoculating step (ii), now limiting the inoculum to microorganisms comprising *Streptococcus thermophilus*. The basis for this limitation is found in claim 7, paragraph [0024] and in the examples.

Furthermore, in claims 1 and 19, Applicants have introduced the feature, respectively, of claims 15 and 20 (both now cancelled) regarding the base of inorganic origin which is now selected from the group consisting of sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, calcium carbonate and ammonia.

Dependent claims 2-3, 10-13 and 16-18 now employ the language of independent claim 1.

Dependent claims 21-24 have been added regarding the further microorganisms that could be present in mixture with *S. thermophilus*. The basis for this is to be found in paragraph [0024], claim 7 and the examples.

Claim Objections

The informalities noted by the Examiner in claims 19 and 20 were typographical errors and have been corrected as suggested by the Examiner.

Claim Rejections – 35 USC § 112

Claims 1-3, 5-18 and 20 have been rejected for omitting essential "providing/contacting" and "concluding/correlating steps." Applicants appreciate the Examiner's sample claim suggestion that should overcome these rejections. Therefore, the language proposed by the Examiner has been adopted.

Claims 16 and 17 have been rejected for insufficient antecedent basis because of the recited limitations "the biomass". To overcome this rejection the word "a biomass" has been introduced in claim 1-step (iii).

Claims 1 and 18 have been rejected for being indefinite, because claims 1 and 18 are unclear. To overcome this rejection claim 1 has been amended by changing the language from "not subjected to any preliminary removal of the protein portion of milk" to "not subjected to any preliminary removal of the protein portion of milk <u>or milk serum</u>", which finds support in the specification at page 1, paragraph [0004].

Accordingly, the § 112, second paragraph, rejections have been overcome and should be withdrawn.

Claim rejections – 35 USC § 102

Claims 1-3, 5, 6, 10-15 and 18-20 stand rejected under 35 U.S.C. § 102(b) as anticipated by Torino, M.I., "Heterofermentative pattern and exopolysaccharide production by *Lactobacillus helveticus* ATCC 15807 in response to environmental pH", Journal of Applied Microbiology, 2001(91) 846-852. This rejection is respectfully traversed.

The Torino reference teaches how the heterofermentative pattern of *Lactobacillus helveticus* ATCC 15807 is influenced by pH.

The presently claimed invention recites a method for preparing galactose from milk or milk serum, inoculating said milk or milk serum with wild-type microorganisms comprising *Streptococcus thermophilus* (and mixtures thereof), and fermenting under controlled pH conditions by adding a base of inorganic origin.

Torino is silent with respect to heterofermentative pattern of *Streptococcus thermophilus* and mixture thereof. Therefore, the presently claimed invention is novel and distinguishes over Torino. Thus, the rejection for anticipation under § 102(b) has been overcome and should be withdrawn.

Claim rejections – 35 USC § 103

Claims 1-3, 5-7 and 10-20 stand rejected under 35 U.S.C. § 103(a) over Acuna, G. et al. "On-line estimation of biological variables during pH controlled lactic acid fermentations", Biotechnology and Bioengineering 1994, 44(10), 1168-1176 and Moore, U.S. 2,974,044 and Turner, K. and Martley, F. "Galactose fermentation and classification of *Thermophilic Lactobacilli*", Applied Environmental Microbiology 1983, 45(6), 1932-1934. This rejection is respectfully traversed.

The problem to be solved by Applicants is to provide a method for preparing galactose in high purity and with high yields which is directly employable in the food industry and in chemical synthesis.

Acuna teaches (for utility in processes for the propagation of lactic starters, production of lactic acid, manufacture of cheese and fermented milk), the indirect measurement of lactose, galactose, lactic acid and biomass concentration from on-line NaOH weight measurements obtained by fermenting a milk serum composition comprising milk whey, 40g/L lactose and yeast, with microorganism cultures of pure *S. Thermophilus 404* and *L. Bulgaricus 398* and mixture under pH-controlled (6.5, 5.8 and 6.5, respectively) by adding NaOH and temperature-controlled (40, 44 and 42°C respectively) for 5-7 hours. Lactose, galactose and lactic acid were analytically quantified using high-pressure chromatography (HPLC). Each sample was precipitated by treating a sample with trichloroacetic acid and centrifuged.

Moore teaches a method for the production of carotenoids by means of fementation processes wherein the pH of the fermentation media, where acids may accumulate, may be adjusted by the addition of NaOH, KOH, $Ca(OH)_2$, NH_4OH, Na_2CO_3, etc. It has absolutely nothing to do with galactose production or lactic acid fermentations.

Turner teaches that the ability to ferment galactose is a major characteristic which can be used to differentiate *Lactobacilus helveticus* (gal+) from *Lalctobacillus lactis* and *Lactobacillus bulgaricus* (gal-). *L. bulgaricus*, commercially available as starter cultures, is, in turn, classified as gal+ (see Table 1 note c). In milk cultures, gal+ strains produce D- and L-lactic acid with little galactose accumulation, whereas gal- strains produce D-lactic acid with galactose accumulated in high levels.

Turner teaches fermenting the above mentioned gal- and gal+ strains for 24 hours at 37°C and detecting (not controlling) a pH value of 3.81±0.24 for gal+, and a pH value of 4.00±0.15 for gal- strains. Turner also mentions that *Streptococcus thermophilus* is ***incapable of fermenting galactose produced from lactose*** and it is known to be classified as a gal- strain. Moreover, Turner teaches that *S. thermophilus* is commonly mixed with gal+ for the manufacture of Swiss and Italian varieties of cheese, while it is commonly mixed with gal- strains for yogurt manufacture (but does not provide details of times and pH condition suitable for these bacterial combinations that would result in the production of galactose in high yield associated with the lowest level of lactose and glucose). Nothing at all is said about *L. casei* classification.

The presently claimed invention is directed to a method for preparing galactose from milk or milk serum (not containing yeast), inoculating said milk or milk serum with wild-type microorganisms comprising *S. thermophilus*, thereby providing a suspension, and fermenting said suspension while maintaining the pH at a constant value between 5 and 7.5 for a period of time between 16 and 24 hours by adding a base of inorganic origin, then acidifying the suspension by stopping the addition of base and allowing the fermentation to proceed for a period of between 5 and 60 hours, whereby a suspension

enriched in galactose is obtained from which a biomass is removed thus providing a solution enriched in galactose.

The so-obtained solution has a galactose content of around 90% (with a negligible/undetectable content of lactose and glucose) which is directly employable in the food industry or chemical synthesis without any further purification or directly crystallisable.

The unexpected technical feature of the claimed invention resides in the use of wild-type microorganisms comprising *S. thermophilus* in a precise combination of times and pH-controlled conditions that lead to the production of galactose in surprisingly high yields and high purity with the use of simple operations. It is implicitly clear that the galactose is obtained in such high purity and yields, using simple procedure (not requiring complex purification techniques, such as chromatography) and low cost starting material (dairy industry waste which is used as such), by mean of an unobvious method which is economically advantageous and hence easily and readily scaled up to a multi-kgs scale in the chemical synthesis industry.

The Examiner's rejection is based on the combination of three (3) references. However, the Applicants do not see any teachings in these references that would direct one of ordinary skill in the art to the claimed combination. Applicants cannot see how or why teachings related to cheese, yogurt and carotenoids would or should have been taken into account by one of ordinary skill in the art of carbohydrate chemistry who was seeking to produce galactose. Surely, the person of ordinary skill in carbohydrate chemistry cannot be said to possess skill in cheese, yogurt and carotenoids production and would not be expected to look to such non-analogous art for a solution to his problem.

Applicants also wish to point out that the need to rely on a combination of three (3) references, besides being, among other things, irrelevant to the invention, provides strong evidence of unobviousness. Even when the three (3) documents are combined, the method of the present invention is not obviously derived as will be evident from the following arguments.

As the Examiner stated, Acuna is silent with respect to the consumption and residue of glucose and what happens when fermenting for times >7 hours. Therefore, Acuna does not teach at what times there will result a higher galactose concentration associated with the lowest lactose and glucose concentration, which is the critical point at which the addition of base must end in order to result in a galactose solution of high purity and high yield. Moreover, Acuna is silent with respect to the fermentations, which after a period of time, while the pH is controlled by adding NaOH, are left to proceed by stopping the base addition thereby spontaneously acidifying without controlling the pH. (This step in the claimed method allows further reduction of the lactose and glucose content while leaving the galactose content unchanged.) If the pH had been further controlled by the further addition of base, the galactose would have been consumed by microorganisms. Acuna teaches stopping the reaction mixture after 5-7 hours by adding trichloroacetic acid which is not employed in the presently claimed method.

Moore's teaching, according to the Examiner, is to add inorganic bases to control pH during fermentations wherein an acid is accumulated. From the Acuna reference the use of NaOH would have been obvious (to anyone that has a basic knowledge of chemistry) and also that other bases equivalent to NaOH could be used for *S. Thermophilus* (and mixtures thereof) fermentations. Therefore, in Applicants' opinion, the Moore reference is not at all on point with respect to the inventive aspect of the presently claimed method which is the easy and economical employment of wild-type microorganisms comprising *S. Thermophilus* for the production of galactose in such high purity and yields that it could be scaled up in the chemical synthesis industry.

Turner is silent with respect to the conditions for *S. thermophilus* fermentation (Turner just discloses conditions for *L. bulgaricus, L. lactis* and *L. helveticus* strains under uncontrolled-pH conditions) and, in particular, is silent with respect to the times and pH that should be applied to achieve better fermentation conditions for this microorganism alone or in mixture with other lactobaccilli.

Turner is also silent with respect to the residual lactose and glucose (which is a critical point of the present invention). Therefore, it is not seen that when Turner is

combined with Acuna what periods of time and what pH conditions would then be taught to one of ordinary skill in the art for the production of galactose associated with the lowest level of lactose and glucose. The optimization of these conditions would have been beyond the routine optimization of conditions since microorganisms have their own multi-dependent fermentation pattern, and matters are further complicated when a mixture of microorganisms of different strains are employed, whose survival in the same culture can both be competitive.

None of the combinations, give a clear indication, without the burden of undertaking undue experimental efforts as to how to solve the problem of providing a method for producing galactose in high yield and purity that could be scaled-up economically in the chemical synthesis industry. It is only by the claimed method that the solution is provided.

The combination of references relied upon by the Examiner does not teach or suggest the claimed method of producing galactose in high yield and purity economically in the chemical synthesis industry and, as such, clearly distinguishes over such combination.

Since a *prima facie* case of obviousness under 35 U.S.C. § 103(a) has not been established by the Examiner, withdrawal of the rejection is respectfully solicited.

Applicants submit that a Notice of Allowance is now in order.

Please charge any fees which may be due and which have not been submitted herewith to our Deposit Account No. 01-0035.

Respectfully submitted,

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